DEPARTMENT OF HEALTH AND HUMAN SERVICES

Agency for Healthcare Research and Quality

Supplemental Evidence and Data Request on Genitourinary Syndrome of Menopause

AGENCY: Agency for Healthcare Research and Quality (AHRQ), HHS.

ACTION: Request for Supplemental Evidence and Data Submissions.

SUMMARY: The Agency for Healthcare Research and Quality (AHRQ) is seeking scientific information submissions from the public. Scientific information is being solicited to inform our review on *Genitourinary Syndrome of Menopause,* which is currently being conducted by the AHRQ's Evidence-based Practice Centers (EPC) Program. Access to published and unpublished pertinent scientific information will improve the quality of this review.

DATES: *Submission Deadline* on or before [INSERT DATE 30 DAYS AFTER DATE OF PUBLICATION IN THE FEDERAL REGISTER].

ADDRESSES:

E-mail submissions: epc@ahrq.hhs.gov

Print submissions:

Mailing Address:

Center for Evidence and Practice Improvement

Agency for Healthcare Research and Quality

ATTN: EPC SEADs Coordinator

5600 Fishers Lane

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Rockville, MD 20857

Shipping Address (FedEx, UPS, etc.):

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FOR FURTHER INFORMATION CONTACT: Jenae Benns, Telephone: 301-427-1496 or Email: epc@ahrq.hhs.gov.

SUPPLEMENTARY INFORMATION: The Agency for Healthcare Research and Quality has commissioned the Evidence-based Practice Centers (EPC) Program to complete a review of the evidence for *Genitourinary Syndrome of Menopause.* AHRQ is conducting this systematic review pursuant to Section 902 of the Public Health Service Act, 42 U.S.C. 299a.

The EPC Program is dedicated to identifying as many studies as possible that are relevant to the questions for each of its reviews. In order to do so, we are supplementing the usual manual and electronic database searches of the literature by requesting information from the public (e.g., details of studies conducted). We are looking for studies that report on

Genitourinary Syndrome of Menopause, including those that describe adverse events. The entire research protocol is available online at:

https://effectivehealthcare.ahrq.gov/products/genitourinary-syndrome/protocol

This is to notify the public that the EPC Program would find the following information on Genitourinary Syndrome of Menopause helpful:

- A list of completed studies that your organization has sponsored for this indication. In the list, please *indicate whether results are available on ClinicalTrials.gov along with the ClinicalTrials.gov trial number*.
    - *For completed studies that do not have results on ClinicalTrials.gov*, a summary, including the following elements: study number, study period, design, methodology, indication and diagnosis, proper use instructions, inclusion and exclusion criteria, primary and secondary outcomes, baseline characteristics, number of patients screened /eligible /enrolled /lost to follow-up /withdrawn /analyzed, effectiveness/efficacy, and safety results.
- *A list of ongoing studies that your organization has sponsored for this indication*. In the list, please provide the ClinicalTrials.gov trial number or, if the trial is not registered, the protocol for the study including a study number, the study period, design, methodology, indication and diagnosis, proper use instructions, inclusion and exclusion criteria, and primary and secondary outcomes.
- Description of whether the above studies constitute *ALL Phase II and above clinical trials* sponsored by your organization for this indication and an index outlining the relevant information in each submitted file.

Your contribution is very beneficial to the Program. Materials submitted must be publicly available or able to be made public. Materials that are considered confidential; marketing

materials; study types not included in the review; or information on indications not included in the review cannot be used by the EPC Program. This is a voluntary request for information, and all costs for complying with this request must be borne by the submitter.

The draft of this review will be posted on AHRQ's EPC Program website and available for public comment for a period of 4 weeks. If you would like to be notified when the draft is posted, please sign up for the e-mail list at: https://www.effectivehealthcare.ahrq.gov/email-updates.

The systematic review will answer the following questions. This information is provided as background. AHRQ is not requesting that the public provide answers to these questions.

Key Questions (KQ)

KQ 1: What is the effectiveness and harms of screening strategies to identify GSM in postmenopausal women? Does screening impact patient reported symptoms or improve quality of life?

KQ 2: What is the effectiveness and comparative effectiveness of hormonal, non-hormonal, and energy-based interventions when used alone or in combination for treatment of GSM symptoms? Which treatments show improvement for which symptoms?

KQ 3: What are the harms (and comparative harms) of hormonal, non-hormonal, and energy-based interventions for GSM symptoms?

KQ 4: What is the appropriate follow-up interval to assess improvement, sustained improvement, or regression of symptoms of GSM in women treated with hormonal, non-hormonal, and energy-based interventions?

KQ 5: What is the effectiveness, comparative effectiveness, and harms of endometrial surveillance among women who have a uterus and are using hormonal therapy for GSM?

Population, Intervention, Comparator, Outcome, Timing, Setting/Study Design (PICOTS)

	Inclusion	Exclusion
Population		
KQ1:	Postmenopausal women	
KQ2-4:	Postmenopausal women, premenopausal women in hypoestrogenic state, or gender diverse individuals on hormonal therapy, with one or more symptom of GSM	Individuals with genitourinary symptoms for reasons other than GSM
KQ5:	Patients with a uterus using hormonal therapy primarily for GSM symptoms	Patients using hormonal therapy for reasons other than GSM
Interventions		
KQ1:	Screening evaluations and/or questionnaires	Physical exam
KQ2-4:	***Hormonal Interventions****:* Systemic estrogen for GSM, vaginal estrogen therapy, including vaginal cream, tablets, inserts or ring, selective estrogen receptor modulator (SERM), intravaginal dehydroepiandrosterone (DHEA), vaginal testosterone, compounded and bioidentical hormonal therapies; phytoestrogens ***Energy-based interventions****:* CO2 laser, Erbium: YAG, radio-frequency laser ***Non-hormonal interventions****:* Over-the-counter non-hormone vaginal lubricants and moisturizers, hyaluronic acid, herbal therapies/supplemental alternatives, vitamin D, vitamin E, probiotics, oxytocin vaginal gel, pelvic floor physical therapy to treat vaginal or sexual symptoms of GSM. ***For KQ4.*** Assess different durations of follow-up	Menopausal hormone therapy only for reasons other than GSM, Laser therapy for anatomic areas other than the vagina, Pelvic floor physical therapy for urinary incontinence
KQ5:	Endometrial surveillance with ultrasound or biopsy	
Comparison		
KQ1:	Usual care	
KQ2-4:	***Effectiveness****:* Placebo, inactive control, sham ***Comparative Effectiveness****:* Another hormonal, non-hormonal, or energy-based intervention ***For KQ4.*** Assess different durations of follow up	
KQ5:	Usual care, or different type or level of surveillance	

Outcomes		
KQ1:	Diagnosis of GSM, potential harms: misdiagnosis as another condition with similar presentation such as inflammatory dermatologic conditions, malignancy, infections, or presence of symptoms prior to menopause. Progressing to unnecessary diagnostics for the index patient such as vaginal or endometrial biopsy.	
KQ 1, 2&4	Change in symptoms: ***Genitourinary symptoms***: urinary frequency, urinary urgency, nocturia, dysuria, recurrent urinary tract infections ***Other urinary symptoms*** (outcomes evaluated for interventions other than PFMT): urinary urge incontinence, overactive bladder ***Genital signs and symptoms***: urethral caruncle, urethral prolapse, vaginal atrophy or atrophic vaginitis, vaginal dryness, vaginal / vulvar irritation, vaginal soreness, vaginal lubrication, vaginal pain ***Sexual symptoms***: dyspareunia, orgasmic dysfunction, low libido, decreased arousal, sexual desire, sexual function, bleeding associated with sexual activity ***Psychological symptoms***: depression, anxiety, quality of life, partner satisfaction	Serum hormone concentration, Stress incontinence
KQ3&5:	***Safety outcomes****:* breast cancer, breast cancer recurrence or progression, breast tenderness, cardiovascular risk, endometrial cancer (KQ5), post-menopausal bleeding (KQ5), endometrial hyperplasia (KQ5), endometrial thickness (KQ5) ***Adverse events****:* worsening or onset of urinary, genital, or sexual symptoms: vaginal burning, vaginal bleeding, vaginal discharge, vaginal scarring, vaginal stenosis; pelvic pain; dyspareunia; urethral strictures; meatal stricture/stenosis. ***Systemic adverse events****:* chronic pain, stroke; VTE (DVT or PE); death; hot flashes; headache; breast pain; cramps; bloating; nausea; vomiting	
Timing		
All KQ	Intervention: any Outcomes: any	
Setting		
All KQ	Any	
Study design		
KQ1	RCTs and prospective observational studies with concurrent comparison group and analytic techniques to control for sample selection bias; systematic reviews of these study designs that assessed ROB of included studies using validated tools.	
KQ2	RCTs or systematic review of RCTs that assessed ROB of included studies using validated tools.	
KQ3	RCTs and prospective observational studies with concurrent comparison group and analytic techniques to control for sample selection bias; systematic reviews of these study designs that assessed ROB of included studies using validated tools.	
KQ4	RCTs or systematic review of RCTs that assessed ROB of included studies using validated tools.	
KQ5	RCTs and prospective observational studies with concurrent comparison group and analytic techniques to control for sample selection bias; systematic reviews of	

	these study designs that assessed ROB of included studies using validated tools.
Language	English only (due to resource limitations)
Geographic Location	Any
Study size	N=20 or more participants analyzed per study arm for RCTs
Publication date	Any

Abbreviations: CO2=carbon dioxide; DHEA=dehydroepiandrosterone; DVT=deep venous thromboembolism; GSM=Genitourinary Syndrome of Menopause; KQ=key question; PE=pulmonary embolism; PFMT=pelvic floor muscle training; RCT=randomized controlled trial; SERM=selective estrogen receptor modulator; VTE= venous thromboembolism

Dated: March 3, 2023.

Marquita Cullom,

Associate Director.

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